

### REMARKS

Claims 40-42, 44-77, 79, and 80 are pending. Claims 45-70 and 72-77 are withdrawn from consideration. Claims 40-42, 44, 71, 79 and 80 have been examined. No claims have been amended.

Applicants note the Examiner's acknowledgement of the priority claim to UK 0224872.2 filed October 25, 2002.

The only remaining rejection of the claims is for obviousness.

#### **Rejections under 35 U.S.C. § 103(a)**

Claims 40-42, 44, 71, and 79 were rejected as unpatentable over U.S. Patent Application No. 2003002215 ("Thinakaran") in view of U.S. Patent No. 4,610,962 ("Takagi"). Applicants traverse.

Claim 40 is directed to a method of detecting the expression and folding of a ble fusion protein by contacting a cell lysate comprising the fusion protein with a surface derivatized with a bleomycin family antibiotic and assessing the binding of the fusion protein to the antibiotic.

Thinakaran does not describe a method in which a lysate comprising a ble fusion protein is contacted with a surface derivatized with a bleomycin family antibiotic, as required by claim 40. In particular, Thinakaran does not describe an *in vitro* binding assay in which a ble fusion protein binds to an antibiotic. The Examiner asserts that it would be reasonable for the skilled person to translate the use of an *in vivo* assay (referring to the selection of high expressing cells using antibiotic) to an *in vitro* assay (referring to the binding assay). However, to the extent Thinakaran teaches *in vitro* methods they are inapposite to Applicant's claimed invention; the skilled person would have no reason to use the *in vitro* binding assays described in Thinakaran to assess the binding of ble to an antibiotic because the specific molecules to which ble binds were already known. Moreover, Thinakaran does not direct the skilled person to adapt *in vivo* binding of ble fusion proteins and antibiotics to an *in vitro* binding assay because the *in vivo* binding is used to select for cells expressing high levels of the fusion protein. Teachings that may be relevant for an *in vivo* assay described in this reference are not

applicable to the claimed *in vitro* methods. Thinakaran's *in vivo* methods require the cells to be living and multiplying for selection to occur.

The Examiner relies on Takagi for its description of substances, including antibiotics, that can be immobilized onto a solid surface. Office action at p. 7, para. 2. The Examiner contends that since Thinakaran describes detecting labelled proteins in an *in vitro* assay, one of ordinary skill would know that an antibiotic can be immobilized on a surface to detect a labelled protein in a binding assay. However, neither Takagi nor Thinakaran provides a reason for making the claimed combination of contacting a lysate comprising a ble fusion protein with an antibiotic-derivatized surface. In the absence of any reason to make the claimed combination there can be no expectation of success in practicing the claimed method. Accordingly, the Examiner has failed to establish a *prima facie* case of obviousness. Applicants request that the rejection be reconsidered and withdrawn.

Claim 80 was rejected as unpatentable over U.S. Patent Application No. 2003002215 ("Thinakaran") in view of U.S. Patent No. 4,610,962 ("Takagi") and in view of Calmels *et al.*, *Molec. Pharmacol.* 44:1135-1141 (1993)("Calmels"). Applicants traverse.

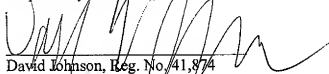
Claim 80 is directed to the method of claim 40 wherein the antibiotic binding to the ble fusion protein is detected by labeling the antibiotic with a marker and detecting binding of the ble fusion protein to the labeled antibiotic by detecting the marker.

The Examiner relies on Calmels for its description of a fluorescently labeled antibiotic and for its teaching, also present in Thinakaran, that ble binds to bleomycin with a 1:1 stoichiometry. Office action at p. 7, last paragraph. Calmels does not overcome the deficiencies of Thinakaran and Takagi discussed above. Accordingly, Applicants request that the rejection be reconsidered and withdrawn.

In summary, the Examiner has failed to establish a *prima facie* case of obviousness with respect to claim 40 and its dependent claims. Applicants request that the rejections of the claims as obvious be reconsidered and withdrawn.

Applicants submit that the application is in condition for allowance and request an action for same. A petition for extension of time accompanies this response. Please charge any additional fees that may be due, or credit any overpayment, to Deposit Account No. 50-0311, Attorney Reference No. ~~40418-508N01US~~.

Respectfully submitted,



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